RAW SEQUENCE LISTING

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) no errors detected.

Application Serial Number:	10/5/6,505
Source:	PUTIO
Date Processed by STIC:	12/14/04

ENTERED

CRF Errors Edited by the STIC Systems Branch

Serial Number: $10/5/6,505$ CRF Edit Date: $12/14/0$ Edited by:
Realigned nucleic acid/amino acid numbers/text in cases where the sequence text "wrapped" to the next line
Corrected the SEQ ID NO. Sequence numbers edited were:
Inserted or corrected a nucleic number at the end of a nucleic line. SEQ ID NO's edited:
Deleted: invalid beginning/end-of-file text ; page numbers
Inserted mandatory headings/numeric identifiers, specifically:
Moved responses to same line as heading/numeric identifier, specifically:
Other:

Revised 09/09/2003



PCT

RAW SEQUENCE LISTING DATE: 12/14/2004
PATENT APPLICATION: US/10/516,505 TIME: 18:17:40

```
1 <110> APPLICANT: ISIS Pharmaceuticals Inc.
      2
              Eric G. Marcusson
              C. Frank Bennett
              Kenneth W. Dobie
      5 <120> TITLE OF INVENTION: ANTISENSE MODULATION OF EXTRACELLULAR-SIGNAL-REGULATED
KINASE-6 EXPRESSION
      6 <130> FILE REFERENCE: PTS-0055WO
      7 <140> CURRENT APPLICATION NUMBER: US/10/516,505
      8 <141> CURRENT FILING DATE: 2004-12-01
      9 <150> PRIOR APPLICATION NUMBER: 10/348,431
     10 <151> PRIOR FILING DATE: 2003-01-17
     11 <150> PRIOR APPLICATION NUMBER: 10/174,465
     12 <151> PRIOR FILING DATE: 2002-06-17
     13 <160> NUMBER OF SEQ ID NOS: 233
     15 <210> SEQ ID NO: 1
     16 <211> LENGTH: 20
     17 <212> TYPE: DNA
     18 <213> ORGANISM: Artificial Sequence
     19 <220> FEATURE:
     20 <223> OTHER INFORMATION: Antisense Oligonucleotide
     21 <400> SEQUENCE: 1
     22
              tccgtcatcg ctcctcaggg
                                                                                     20
     24 <210> SEQ ID NO: 2
     25 <211> LENGTH: 20
     26 <212> TYPE: DNA
     27 <213> ORGANISM: Artificial Sequence
     28 <220> FEATURE:
     29 <223> OTHER INFORMATION: Antisense Oligonucleotide
     30 <400> SEQUENCE: 2
     31
              gtgcgcgcga gcccgaaatc
                                                                                     20
     33 <210> SEQ ID NO: 3
     34 <211> LENGTH: 20
     35 <212> TYPE: DNA
     36 <213> ORGANISM: Artificial Sequence
     37 <220> FEATURE:
     38 <223> OTHER INFORMATION: Antisense Oligonucleotide
     39 <400> SEQUENCE: 3
     40
              atgcattctg cccccaagga
                                                                                     20
     42 <210> SEO ID NO: 4
     43 <211> LENGTH: 1670
     44 <212> TYPE: DNA
     45 <213> ORGANISM: H. sapiens
     46 <220> FEATURE:
     47 <220> FEATURE:
```



DATE: 12/14/2004 PATENT APPLICATION: US/10/516,505 TIME: 18:17:40

48	<221>	NAMI	E/KE	Y: CI	os														
49	<222>	LOCA	OITA	v : (2	34).	(1	137)												
50	<400>	SEQ	JENCI	∃: 4															
51		ggct	tatgo	egg g	ggtg	ggca	gc to	cccg	ggcct	gc	ate	g age	c tc	t cc	g cc	g cc	acc	54	Ł
52										_	Met	t Se	r Se	r Pro	o Pro	o Pro	o Thr		
53												1			!	5			
54		cgc	agt	ggc	ttt	tac	cgc	cag	gag	qtq	acc	aaq	acq	qcc	tgg	qaq	qtq	102	2
55						Tyr													
56		•		10		•	•		15			•		20	-				
57		cqc	qcc	qtq	tac	cgg	qac	ctq	caq	ccc	ata	qqc	tcq	qqc	qcc	tac	ggc	150)
58						Arg													
59		_	25		_		-	30				-	35	•		•	•		
60		gcg	gtg	tgc	tcg	gcc	gtg	qac	qqc	cqc	acc	qqc	qct	aaq	qtt	qcc	atc	198	3
61		-		_	_	Āla				_			_	_	_	_			
62		40		-			45	-	•	J		50		-			55		
63		aag	aag	ctg	tat	cgg	ccc	ttc	cag	tcc	gag	ctq	ttc	qcc	aaq	ctc	qcc	246	5
64						Arg													
65		-	-		-	60					65				-	70			
66		tac	cgc	gag	ctq	cgc	ctq	ctc	aaq	cac	atq	cqc	cac	qaq	aac	ata	atc	294	Ł
67						Arg													
68		-	_		75	J			•	80		-			85				
69		ggg	ctg	ctq	qac	gta	ttc	act	cct	qat	qaq	acc	ctq	qat	qac	ttc	acq	342	2
70						Val													
71		-		90	-				95	•				100	•				
72		gac	ttt	tac	ctq	gtġ	atq	ccq	ttc	atq	qqc	acc	qac	ctq	qqc	aaq	ctc	390)
73						Val													
74		_	105	_				110			-		115		-	-			
75		atg	aaa	cat	gag	aag	cta	ggc	gag	gac	cgg	atc	cag	ttc	ctc	gtg	tac	438	3
76						Lys													
77		120					125	_			_	130					135		
78		cag	atg	atg	aag	ggg	ctg	agg	tat	atc	cac	gct	gcc	ggc	atc	atc	cac	486	5
79		Gln	Met	Met	Lys	Gly	Leu	Arg	Tyr	Ile	His	Ala	Ala	Gly	Ile	Ile	His		
80						140					145			_		150			
81		aga	gac	ctg	aag	ccc	ggc	aac	ctg	gct	gtg	aac	gaa	gac	tgt	gag	ctg	534	Ŀ
82		Arg	Asp	Leu	Lys	Pro	Gly	Asn	Leu	Ala	Val	Asn	Glu	Asp	Cys	Glu	Leu		
83					155					160					165				
84		aag	atc	ctg	gac	ttc	ggc	ctg	gcc	agg	cag	gca	gac	agt	gag	atg	act	582	2
85		Lys	Ile	Leu	Asp	Phe	Gly	Leu	Ala	Arg	Gln	Ala	Asp	Ser	Glu	Met	Thr		
86				170					175					180					
87		ggg	tac	gtg	gtg	acc	cgg	tgg	tac	cgg	gct	CCC	gag	gtc	atc	ttg	aat	630)
88		Gly	Tyr	Val	Val	Thr	Arg	Trp	Tyr	Arg	Ala	Pro	Glu	Val	Ile	Leu	Asn		
89			185					190					195						
90		tgg	atc	gcg	tac	acg	cag	acg	gtg	gac	atc	tgg	tct	gtg	ggc	tgc	atc	678	3
91						Thr													
92		200					205					210					215		
93		atg	gcg	gag	atg	atc	aca	ggc	aag	acg	ctg	ttc	aag	ggc	agc	gac	cac	726	5
94						Ile													
95						220		_	•		225		-	_		230			
96		ctg	gac	cag	ctg	aag	gag	atc	atg	aag	gtg	acg	ggg	acg	cct	ccg	gct	774	Ŀ



PATENT APPLICATION: US/10/516,505 TIME: 18:17:40

DATE: 12/14/2004

97		Leu I	Asp			Lys	Glu	Ile	Met :	_	Val	Thr	Gly	Thr		Pro .	Ala	
98		~-~			235					240					245			000
99 100									agc (822
101		GIU	Pile	250		Arg	ьeu	GIII	Ser 255	Asp	GIU	Ala	ьуѕ		_	мет	гàг	
101		aac	ata			++~	~ 3~		aag	~a+	+++	~~~	++	260			224	870
102									Lys									870
103		GIY	265		Giu	пец	GIU	. цув 270		Asp	PHE	AIG	275	116	ьеu	. 1111	ASII	
105		aca			cta	act	ata		ctc	cta	asa	220		ato	ata	cta	asc.	918
106									Leu									310
107		280	UCI	110	ыси	AIG	285		шец	пец	GIU	290		пец	. vai	пец	295	
108			gac	atc	agg	tta			ggc	gag	+++			cat	CCC	tac		966
109									Gly									200
110					5	300			. 011		305					310	1110	
111		qaq	tcc	cta	cac		acd	gaa	gat	gag			atc	cao	aaq		gat.	1014
112									Asp									
113					315	-			-	320					325	_		
114		gac	tcc	ttt	gac	tac	ttt	gac	cgc	aca	ctg	gat	gaa	tgg	aaq	cqt	gtt	1062
115									Arg									
116			•	330		-			335			_		340	_	_		
117		act	tac	aaa	gag	gtg	ctc	ago	ttc	aag	cct	ccc	cgg:	cag	ctg	ggg	gcc	1110
118		Thr	Tyr	Lys	Glu	Val	Leu	Ser	Phe	Lys	Pro	Pro	Arg	Gln	Leu	Gly	Ala	
119			345					350					355					
120		agg	gtc	tcc	aag	gag	acg	cct	ctg	tga	aga	tctc	tgg	gctc	cggg	gt		1157
121		_	Val	Ser	Lys	Glu			Leu									
122		360					365											
123														_	_		tgacct	1217
124																	gaccct	1277
125																	actttc	1337
126																	acacaa	1397
127								_	_				_	_			ctctga	1457
128 129											_					_	caactc	1517
130									-				_			_	ggaatg tccaaa	1577 1637
131									aaaa	_		aaca	gac		cty	caye	CCCaaa	1670
133 <	210>					aaaa	aa a	aaaa	aaaa	a aa	a							1070
134					-													
135 <																		
136 <					rtif	icia	l Se	quen	ce									
137 <								1										
138 <					MATI	ON:	PCR	Prim	er									
139 <																		
140		_			cctt	gacc	tt											20
142 <	210>					_												
143 <	211>	LEN	GTH:	16														
144 <	212>	TYP	E: D	NA											٠			
145 <					rtif	icia	l Se	quen	ce									
146 <																		
147 <	223>	OTH	ER I	NFOR	MATI	ON:	PCR	Prim	er									



DATE: 12/14/2004 PATENT APPLICATION: US/10/516,505

TIME: 18:17:40

	148	<400>	SEQUENCE: 6	
	149		tggaacccgg gcgtct	16
	151	<210>	SEQ ID NO: 7	
	152	<211>	LENGTH: 24	
	153	<212>	TYPE: DNA	
	154	<213>	ORGANISM: Artificial Sequence	
			FEATURE:	
			OTHER INFORMATION: PCR Probe	
			SEQUENCE: 7	
	158	12007	ttgcatccca aggcatccat caga	24
		<210>	SEQ ID NO: 8	
			LENGTH: 19	
			TYPE: DNA	
			ORGANISM: Artificial Sequence	
			FEATURE:	
			OTHER INFORMATION: PCR Primer	
			SEQUENCE: 8	
	167			19
			gaaggtgaag gtcggagtc SEQ ID NO: 9	13
			LENGTH: 20	
			TYPE: DNA	
			ORGANISM: Artificial Sequence	•
			- · ·	
			FEATURE:	
			OTHER INFORMATION: PCR Primer	
		<400>	SEQUENCE: 9	~ ~
	176	07.0	gaagatggtg atgggatttc	20
			SEQ ID NO: 10	
			LENGTH: 20	
			TYPE: DNA	
			ORGANISM: Artificial Sequence	
			FEATURE:	
			OTHER INFORMATION: PCR Probe	
			SEQUENCE: 10	
	185		caagetteee gtteteagee	20
			SEQ ID NO: 11	
		•	LENGTH: 20	
			TYPE: DNA	
			ORGANISM: Artificial Sequence	
			FEATURE:	
			OTHER INFORMATION: Antisense Oligonucleotide	
•			SEQUENCE: 11	
	194		ccttcatcat ctggtacacg	20
			SEQ ID NO: 12	
	197	<211>	LENGTH: 20	
			TYPE: DNA	
	199	<213>	ORGANISM: Artificial Sequence	
	200	<220>	FEATURE:	
	201	<223>	OTHER INFORMATION: Antisense Oligonucleotide	
	202	<400>	SEQUENCE: 12	

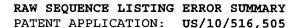


DATE: 12/14/2004 TIME: 18:17:40

Input Set : N:\Crf4\12102004\J516505.raw
Output Set: N:\CRF4\12142004\J516505.raw

PATENT APPLICATION: US/10/516,505

	202			
	203	210	tccttcagct ggtccaggtg	20
			SEQ ID NO: 13	
			LENGTH: 20	
			TYPE: DNA	
			ORGANISM: Artificial Sequence	
			FEATURE:	
			OTHER INFORMATION: Antisense Oligonucleotide	
		<400>	SEQUENCE: 13	
	212	010	ccaccagete tgaggtttet	20
			SEQ ID NO: 14	
			LENGTH: 20	
			TYPE: DNA	
			ORGANISM: Artificial Sequence	
			FEATURE:	
			OTHER INFORMATION: Antisense Oligonucleotide	
			SEQUENCE: 14	
	221		ggagagetea tggeaggeee	20
			SEQ ID NO: 15	
			LENGTH: 20	
			TYPE: DNA	
			ORGANISM: Artificial Sequence	
			FEATURE:	
			OTHER INFORMATION: Antisense Oligonucleotide	
		<400>	SEQUENCE: 15	20
	230	-210-	gtggcgcatg tgcttgagca	20
			SEQ ID NO: 16 LENGTH: 20	
			TYPE: DNA	
			ORGANISM: Artificial Sequence	
			FEATURE:	
			OTHER INFORMATION: Antisense Oligonucleotide SEQUENCE: 16	
	239	(400)	cccttcatca tctggtacac	20
		~210×	SEQ ID NO: 17	20
			LENGTH: 20	
			TYPE: DNA	
			ORGANISM: Artificial Sequence	
			FEATURE:	
			OTHER INFORMATION: Antisense Oligonucleotide	
			SEQUENCE: 17	
	248	(400)	atccagggtc tcatcaggag	20
		-210>	SEQ ID NO: 18	20
			LENGTH: 20	
			TYPE: DNA	
			ORGANISM: Artificial Sequence	
			FEATURE:	
			OTHER INFORMATION: Antisense Oligonucleotide	
			SEQUENCE: 18	
	257	11007	cccggagccc agagatette	20
•	,		coogsageed agagatette	20



DATE: 12/14/2004 TIME: 18:17:41

Input Set : N:\Crf4\12102004\J516505.raw
Output Set: N:\CRF4\12142004\J516505.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

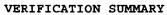
Seq#:71; N Pos. 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20

Seq#:75; N Pos. 727

Invalid Line Length:

The rules require that a line not exceed 72 characters in length. This includes spaces.

Seq#:1; Line(s) 5



PATENT APPLICATION: US/10/516,505

DATE: 12/14/2004 TIME: 18:17:41

Input Set : N:\Crf4\12102004\J516505.raw
Output Set: N:\CRF4\12142004\J516505.raw

L:715 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:71 after pos.:0

L:918 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:75,Line#:0

L:931 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:75 after pos.:720